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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 04/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/085,108	LUCAS ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *07/16/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of group II claim 31, in Paper of 10/21/03 is acknowledged and entered.

Claim 31 is pending in the instant application and Claims 1-30, 32-33 have been cancelled.

Accordingly, claim 31 is examined in the instant application.

CONTINUATION DATA

The continuation data submitted on 05/29/02 have been updated as follows:

This application is a divisional application of Serial No. 09/501,104 filed February 09, 2000, now abandoned, which is a CIP of Application No. 09/468,433 now US Patent No. 6,680,191, which is a CIP of 09/066,281 filed April 24, 1998, now US Patent No. 6,475,783, which is a CIP of Application No. 08/845,528 filed April 25, 1997 now U.S. Patent No. 6,027,924, all of which are incoporated herein in their entirety by reference.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

Claim 31 is rejected under 35 USC 112, first paragraph.

Claim 31 is drawn to method for determining expression of a MAGE-3 gene in a sample, comprising contacting said sample with (i) an oligonucleotide "having" a sequence set forth by nucleotides 175-195 of SEQ ID NO:21 and (ii) an oligonucleotide "having" a sequence that is "complementary" to nucleotides 711-731 of SEQ ID NO:21, under conditions favoring hybridization of the sequences of (i) or (ii) to an MAGE-C3 coding sequence, carrying out polymerase chain reaction and determining expression product to determine presence of an MAGE-C3 coding sequence in said sample.

It is noted that the language "having" could be reasonably interpreted as an open language and has the same meaning as "comprising".

It is further noted that a complement could be partial or full length complement, wherein partial complement could share with nucleotides 711-731 of SEQ ID NO:21 only a few nucleotides.

Claim 31 encompasses method for determining expression of a MAGE-3 gene in a sample, using as primers an oligonucleotide with unknown structure comprising nucleotides 175-195 of SEQ ID NO:21, e.g. an oligonucleotide that has unknown structure 3' of nucleotides 175-195 of SEQ ID NO:21, and an oligonucleotide with unknown structure sharing only a few nucleotides with nucleotides 711-731 of SEQ ID NO:21, which would be expected to hybridize to a whole universe of nucleic acid species, including those that have little or no structural identity to SEQ ID NO:21.

In other words, claim 31 encompasses method for determining expression of a MAGE-3 gene in a sample, using numerous structural oligonucleotide variants.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of oligonucleotide primers for PCR, per Lilly by structurally describing a representative number of or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the

specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe oligonucleotide primers for PCR in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of, nor any physical or chemical characteristics of any oligonucleotide primer, other than an oligonucleotide consisting of nucleotides 175-195 of SEQ ID NO:21 and an oligonucleotide which is a full length complement of an oligonucleotide consisting of nucleotides 711-731 of SEQ ID NO:21, nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses a single pair of primers, i.e. an oligonucleotide consisting of nucleotides 175-195 of SEQ ID NO:21 and an oligonucleotide which is a full length complement of an oligonucleotide consisting of nucleotides 711-731 of SEQ ID NO:21, this does not provide a description of the oligonucleotides used in the claimed method that would satisfy the standard set out in Enzo.

The specification also fails to describe the oligonucleotides by the test set out in Lilly. The specification describes only a single pair of primers, i.e. an oligonucleotide consisting of nucleotides 175-195 of SEQ ID NO:21 and an oligonucleotide which is a full length complement of an oligonucleotide consisting of nucleotides 711-731 of SEQ ID NO:21. Therefore, it necessarily fails to describe a "representative number" of such

species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Since the specification fails to adequately describe the product for use in the claimed method, it also fails to adequately describe the claimed method using said product.

Thus, the specification does not provide an adequate written description of a method for determining expression of a MAGE-3 gene in a sample, using (i) an oligonucleotide "having" a sequence set forth by nucleotides 175-195 of SEQ ID NO:21 and (ii) an oligonucleotide "having" a sequence that is "complementary" to nucleotides 711-731 of SEQ ID NO:21 in a polymerase chain reaction, that is required to practice the claimed invention.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

Claim 31 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method for determining expression of a MAGE-3 gene in a sample, comprising contacting said sample with (i) an oligonucleotide "consisting of " a sequence set forth by nucleotides 175-195 of SEQ ID NO:21 and (ii) an oligonucleotide "consisting of " a sequence that is a "full length complete complement" of a sequence "consisting" of nucleotides 711-731 of SEQ ID NO:21, and carrying out polymerase chain reaction for 30 cycles of 1 min at 94^0C, 1 min at 65^0 C and 3 min at 72^0 C (specification, p.42, first paragraph), **does not reasonably provide enablement for a method for determining expression of a MAGE-3 gene** in a

sample, comprising contacting said sample with **(i) an oligonucleotide "having" a sequence set forth by nucleotides 175-195 of SEQ ID NO:21 and (ii) an oligonucleotide "having" a sequence that is "complementary" to nucleotides 711-731 of SEQ ID NO:21, under conditions favoring hybridization of the sequences of (i) or (ii) to an MAGE-C3 coding sequence**, carrying out polymerase chain reaction. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 31 is drawn to method for determining expression of a MAGE-3 gene in a sample, comprising contacting said sample with (i) an oligonucleotide "having" a sequence set forth by nucleotides 175-195 of SEQ ID NO:21 and (ii) an oligonucleotide "having" a sequence that is "complementary" to nucleotides 711-731 of SEQ ID NO:21, under conditions favoring hybridization of the sequences of (i) or (ii) to an MAGE-C3 coding sequence, carrying out polymerase chain reaction and determining expression product to determine presence of an MAGE-C3 coding sequence in said sample.

It is noted that the language "having" could be reasonably interpreted as an open language and has the same meaning as "comprising".

It is further noted that a complement could be partial or full length complement, wherein partial complement could share with nucleotides 711-731 of SEQ ID NO:21 only a few nucleotides.

In addition, it is noted that conditions favoring "hybridization" of the sequences of (i) and (ii) to an MAGE-C3 coding region encompasses any hybridization conditions,

from low to high stringent conditions, wherein under very low stringent unrelated sequences are expected to hybridize to MAGE-C3.

Moreover, the language "determining expression of a MAGE-C3 gene" encompasses "determining expression of variant of MAGE-C3 gene"

Claim 31 encompasses method for determining expression of a MAGE-3 gene in a sample, comprising contacting with a sample an oligonucleotide with unknown structure comprising nucleotides 175-195 of SEQ ID NO:21, e.g. an oligonucleotide that has unknown structure 3' of nucleotides 175-195 of SEQ ID NO:21, and an oligonucleotide with unknown structure, sharing only a few nucleotides with nucleotides 711-731 of SEQ ID NO:21, under low stringent hybridization conditions, and carrying out polymerase chain reaction.

In other words, claim 31 encompasses method for determining expression of a MAGE-3 gene in a sample, using numerous structural oligonucleotide variants.

The specification discloses PCR of MAGE-C3 using as sense primer nucleotides 175-196 of SEQ ID NO:21 and anti-sense primer of nucleotides 711-731 of SEQ ID NO:21 (p.42, first paragraph).

The specification does not disclose how to make numerous oligonucleotide variants for use in the claimed method, such that MAGE-C3 of SEQ ID NO:21 could be detected.

One cannot extrapolate the teaching in the specification to the scope of the claim. One would not know how to make the oligonucleotide variants such that MAGE-C3 is detected using said oligonucleotides in polymerase chain reaction, in view of a

lack of a teaching of how to make said structural oligonucleotide variants. Further, one would have expected that using the oligonucleotides encompassed in the claim, unrelated sequences would be detected, because the oligonucleotides are not specific for SEQ ID NO:21 and would be misprimed, permitting hybridization of unrelated sequence. In other words, the claimed method would be non-specific for MAGE-C3 of SEQ ID NO:21, and would detect unrelated sequences.

Further, even if the oligonucleotides in the claimed methods are specific for SEQ ID NO:21, i.e. an oligonucleotide "consisting of " a sequence set forth by nucleotides 175-195 of SEQ ID NO:21 and an oligonucleotide "consisting of " a sequence that is a "full length complete complement" of a sequence "consisting" of nucleotides 711-731 of SEQ ID NO:21, using the claimed method having the recited hybridization conditions, one would expect that unrelated sequences would be detected. As conventionally understood in the art and as taught by US Patent No. 5,912,143, hybridization is used to refer to any process by which a strand of nucleic acid binds with a complementary strand through base pairing (col 5, lines 3-5) and further teaches that numerous equivalent conditions may be employed to comprise either low or high stringency conditions and hybridization solutions my be varied to generate conditions of either low or high stringency (col 5, lines 57-67). The stringent conditions claimed read on both high and low stringency conditions. It is well known that the lower the stringency condition the more dissimilar the hybridizing molecule will be from the molecule to which it hybridizes. For example, Sambrook et al, eds, 1989, 2nd ed, Molecular Cloning, a laboratory manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, p. 11.52,

teach that the temperature of hybridization, (which is related to the degree of stringency) should be high enough to suppress hybridization of the probe to incorrect sequences. Sambrook et al further teach that if the probe hybridizes indiscriminately, repeat the hybridization at a higher temperature or wash under conditions of higher stringency (p. 11.52, last two lines).

When given the broadest reasonable interpretation, the oligonucleotides in the claimed method would hybridize to unrelated sequence, and thus the claimed method would detect unrelated sequences.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

MINH TAM DAVIS

PATENT EXAMINER

January 20, 2004